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NOVEL UNCATALYSED MICHAEL REACTIONS OF LITHIUM TRIALKYLALKYNYLBORATES WITH ALKYLIDENEMALONATES AND ALKYLIDENEACETOACETATES.

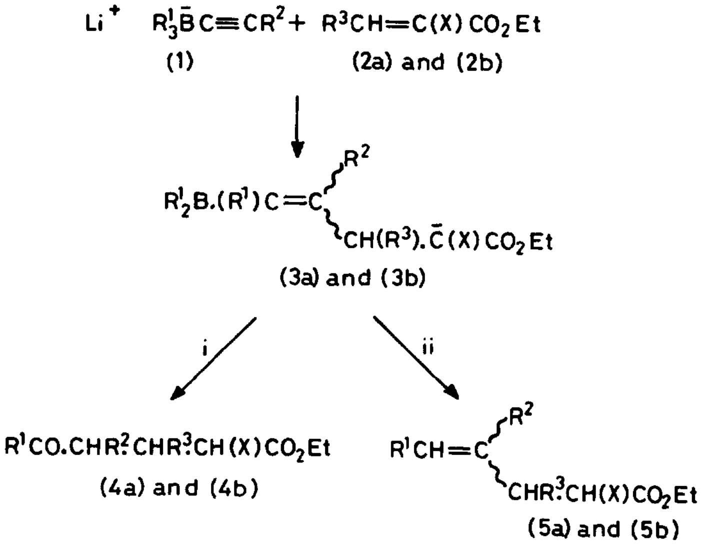
Andrew Pelter* and J. Madhusudhana Rao.

Department of Chemistry, University College of Swansea, Singleton Park,
Swansea SA2 8PP, U.K.

Summary. Alkynylborates and alkylidenemalonates and alkylideneacetoacetates undergo unusual Michael reactions which involve migration of alkyl groups from boron to carbon, to yield products of synthetic value.

We have previously reported[1] that trialkylalkynylborates (1) interact with αβ-unsaturated nitro-compounds in a Michael reaction that is unique[2] in that migration of an alkyl group from boron to carbon is a necessary condition of reaction.

It is now clear that this was merely the first of a new generic type of Michael reaction as the salts (1) react in a similar fashion with a large number of Michael acceptors leading to products of potential in organic synthesis (see Scheme).



(a) $X = CO_2Et$; (b) $X = COCH_3$

i, m-Chloroperbenzoic acid; ii, Pr^iCO_2H in THF.

Scheme

We were not able to obtain an uncatalysed reaction with monofunctional compounds CH_2=CHX (X = CO_2Et, $COCH_3$*) in which CH_3X has pK_A 20-25.[3] Nor could reaction be induced with 2-cyclopentenone and 2-cyclohexenone. However with compounds RCH=CXY (2) (a, X = Y = CO_2Et; b, X = CO_2Et, Y = $COCH_3$) in which the pK_A of CH_2XY is between 9 and 11 (n.b. CH_3NO_2 has pK_A 10) smooth high yielding reactions were obtained. On this basis alkylidenecyanoacetates and alkylidenemalondinitriles should also react smoothly (pK_A $CH_2(CN)_2$ = 11, pK_A $CH_2(CN)CO_2Me$ = 9).

Addition to alkylidenemalonates and acetoacetates is equivalent to addition to the monofunctional alkenes in that the final products can be decarboxylated.

The intermediate alkenylboranes (3) (Scheme) obtained in the Michael reactions can be oxidised to 1,5-ketoesters (4) and hydrolysed to γδ-unsaturated esters (5). Initially the oxidation was troublesome but, in general, use of m-chloroperbenzoic acid leads to the desired ketones without hydrolysis of the ester groupings.

Typical results are given in Tables 1 and 2 which show the generality and limitations of the reactions.

Table 1.

Yields[a] of products from Michael addition-oxidation of (1)[b]

R^1	R^3	X	Yield (%) of (4)
Hexyl	Me	CO_2Et	91
Hexyl	Ph	CO_2Et	83
Hexyl	H	CO_2Et	67
Hexyl	Me	$COCH_3$	74
Hexyl	Ph	$COCH_3$	79
Cyclopentyl	Me	CO_2Et	67[c]

a) All yields are of isolated characterised products based on alkyne.

b) R^2 = Bu^n in all cases. c) Oxidation with NaOAc/H_2O_2 for 75h at 25°C G.c. yield of 84%.

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* Following our earlier report, A. Suzuki, (Chem.Letters, 1980, 221) has recently noted a Lewis acid catalysed reaction with methyl vinyl ketone which gave 24% yield of 1,5-diketone in our hands.

Table 2.

Yields of products from Michael addition-hydrolysis of (1).

R^1	R^2	R^3	X	Yield (%)^a of (5)	Ratio of isomers^b
Hexyl	Butyl	Me	CO_2Et	80	64:34
Octyl	Butyl	Me	CO_2Et	93	67:33
Hexyl	Hexyl	Me	CO_2Et	88	68:32
Hexyl	Butyl	Ph	CO_2Et	82	75:25
Hexyl	Butyl	H	CO_2Et	84	73:27
Hexyl	Butyl	Me	$COCH_3$	75	78:22
Hexyl	Butyl	Ph	$COCH_3$	80	67:33
Cyclopentyl	Butyl	Me	CO_2Et	72	64:36^c
Phenyl	Butyl	Me	CO_2Et	0	-

a) All yields are of isolated characterised products based on alkyne. b) Isomer with C-5 at lower field in the ^{13}C n.m.r. given first. c) Refluxed in THF with isobutyric acid for 44h.

We would detect little difference between the rates of Michael additions (ca. 1h. required for $R^{p}_{3}\bar{B}C{\equiv}CR^{1}$) for the (a) and (b) series. Nor is any appreciable difference in work-up procedure required. However when a tri-sec-alkylalkynylborate is used at least 17h. is required for the Michael addition. This is a kinetic effect and does not reflect migratory aptitudes, as when lithium dicyclohexyl- and di-2-methylcyclohexyl-n-hexylhexynylborates are reacted with $CH_3CH{:}C(CO_2Et)_2$ mixtures result which lead to a migratory aptitude of 0.35 and 0.11 for the cyclohexyl and 2-methylcyclohexyl groups respectively as compared with n-hexyl.

Oxidations using m-chloroperbenzoic acid gave rise to 1,5-keto-esters (4) (Scheme) in excellent yields in most cases. However in the case of 3a (R^1 = cyclopentyl, R^3 = Me) peracid oxidation failed and buffered hydrogen peroxide over a long period (see Table 1) was used instead. This latter oxidant had only given poor yields (ca. 20%) with all the previous migration products, 3 (R^1 = prim-alkyl).

In general hydrolysis was accomplished using degassed isobutyric acid in THF at room temperature for 20h. Again considerably stronger conditions are required with 3a (R^1 = cyclopentyl, R^3 = Me) (see Table).

Electrophilic attack by the Michael acceptor on the triple bond of the alkynylborates is not stereospecific (Table 2), the mixture of isomers resulting being very similar to that produced by the simple alkylation of alkynylborates.[4]

It is interesting that no reaction product could be obtained from the Michael reaction-hydrolysis sequence involving lithium triphenylhexynylborate (Table 2) even though isobutyric acid in refluxing diglyme was eventually used for the hydrolysis.

The reaction suffers the usual limitations of uncatalysed Michael reactions in that if the Michael acceptor is geminally disubstituted (e.g. $Me_2C:CH.CO_2Et$) then reaction is inhibited. However the large number of acceptors for which it is successful including our previously reported αβ-unsaturated nitro-compounds, show that this unusual type of Michael reaction has wide applicability and synthetic potential.

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